Beecham Biologicals in 1996. Currently, he is a group research leader and works as an immunologist studying HIV and other diseases.

In rejecting the application, the Examiner lists obstacles to vaccine development and therapeutic approaches with regard to retroviruses associated with AIDS in humans. These obstacles, in turn, allegedly preclude one of ordinary skill in the art from accepting any vaccine, immunization treatment, or therapeutic regimen on its face. Thus, the Examiner requires—as a condition of enablement—that the Applicant submit either *in vivo* or *in vitro* data to show that the claims are enabling. The Examiner, relying on Haynes, states that as no animal model is available for studying AIDS-associated retroviruses, the Applicants' specification cannot be enabling. Specifically, the Examiner bases rejection on the fact that the chimpanzees, while capable of becoming infected with HIV, do not develop full blown AIDS symptoms. However, the Voss declaration traverses the Examiner's rejection because it shows that one such animal model is in fact available for studying anti-HIV vaccines.

The Voss declaration traverses the Examiner's rejection because it does not base its research on the chimpanzee model. Rather, the Applicants submit clinical data based on the rhesus monkey model. Unlike the chimpanzee, the rhesus monkey is capable of developing AIDS-like symptoms from viral exposure to SHIV (Voss at p. 3). Further, as the Voss declaration states, the rhesus monkey is the best model for researching anti-HIV vaccines (Voss at p. 3). Thus, under Hartop, the Applicant's data shows that its invention meets the statutory requirement for patentability.

In a clinical research study, eight Rhesus monkeys were challenged with SHIV. Four monkeys were in the control group while the other four were vaccinated. Two of the vaccinated

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Rhesus monkeys were ultimately protected from SHIV infection while all members of the control group became infected (Voss, Table 6). Due to the lack of a fully characterized assay system with appropriate control samples, the data regarding CTL levels in the Rhesus Monkeys were not interpretable. Nevertheless Applicants' invention protected half of the experimental group.

The Examiner also rejects the application arguing that applicant's invention, whereby cytolytic responses are synergistically enhanced, is not directly correlative to protection from HIV infection. The Examiner cites the study of Butini demonstrating that the existence of high CTL activity in humans with HIV was not predictive of protection or the slowing of disease progression. The Examiner also cites Fox stating that "no single therapy has emerged as a sure winner in the campaign against HIV." The Applicants respond that recent research shows that in fact high CTL levels are critical in protecting humans from HIV infection (Walker, Rinaldo Voss at p. 2). Anti-HIV vaccine research is thus now focused on generating a high CTL response. Therefore, one of ordinary skill in the art would recognize and accept the approach of boosting CTL levels as a scientifically sound approach for combating HIV infection. Such increased levels were seen in the murine model after vaccination (Voss at p. 4). A vaccine containing the QS21 and 3D-MPL adjuvants was administered to mice on two occasions. Serological testing showed that the Applicants' vaccine succeeded in generating a strong CTL response (Voss at p. 3, tables 1-3).

Data from Phase I clinical trials is also provided to the Examiner. It is critical to note that Phase I trials are *not* designed to test a vaccine's efficacy. As Haynes teaches, the purpose of Phase I clinical trials is not to measure the efficacy of a vaccine, instead its purpose is to test the

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vaccine for safety and immunogenicity in small numbers of low-risk individuals. The vaccine successfully completed Phase I clinical trials. That no CTL8+ response was measured is irrelevant. As the Voss declaration demonstrates numerous factors may account for the lack of a CTL8+ response: selective population in a particular region of the body, poor timing of CTL8+ sampling, lack of positive control samples, and a limited test group (Voss at p. 5). The CTL level was tested only because the opportunity presented itself, and it was not a goal of the study to measure or detect CTL. Thus, the failure to detect CTL in a phase I test is not indicative of the vaccine efficacy.

The Applicants have performed cytokine research studies indicating that their invention stimulates a very strong Th1-type cytokine response in mice. According to the Voss declaration, CTL responses are normally associated with strong Th-1 type responses and are indeed may be considered a subset of Th-1 type responses (Voss at p. 7). Voss also hypothesizes that, in addition to CTL, other Th-1 type effector components may play a role in protecting from HIV infection. The Applicants' invention advantageously increases both CTL levels and Th-1 production. Further, this dual increase is expected to occur in HIV vaccines containing both the QS21 and 3D-MPA adjuvants.

In sum, the Applicants traverse the Examiner's rejection for the following reasons. First, the Applicants show that an acceptable animal model for studying anti-HIV vaccines exist and is recognized by those of ordinary skill in the art. Second, those of ordinary skill in the art also recognize that high CTL levels are indicative of anti-HIV therapy and are the focus of HIV vaccine research. Third, the Applicants' invention does boost CTL levels in the murine model and prevented SHIV infection in Rhesus monkeys. Fourth, the Applicants' invention has

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successfully completed Phase I clinical trials, and finally, in addition to generating a CTL response in mice, the invention also stimulates a very strong Th-1 type response.

In view of the foregoing remarks, Applicants respectfully request the reconsideration and reexamination of this application and the timely allowance of the pending claims.

To the extent if any further extension of time under 37 C.F.R. § 1.136 is required to obtain entry of this response, such extension is hereby respectfully requested. If there are any fees due under 37 C.F.R. §§ 1.16 or 1.17 which are not enclosed herewith, including any fees required for an extension of time under 37 C.F.R. § 1.136, please charge such fees to our Deposit Account No. 06-0916.

Respectfully submitted,

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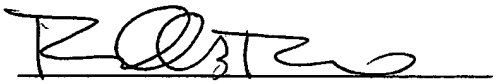
By: 

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